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10/568,729	07/13/2006	Neil Cashman	15289-8	7149

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EXAMINER	
WANG, CHANG YU	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
12/29/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,729	CASHMAN ET AL.	
	Examiner	Art Unit	
	CHANG-YU WANG	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11-14,16-27 and 29-56* is/are pending in the application.

4a) Of the above claim(s) *3-8,18,19,23-27,31-38,40,42-46 and 50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 9, 11-14, 16-17, 20-22, 29-30, 39, 41, 47-49 and 51-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/15/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RESPONSE TO AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/9/09 has been entered.

Status of Application/Amendments/claims

2. Applicant's amendment filed 10/9/09 is acknowledged. Claims 10, 15 and 28 are cancelled. Claims 1, 2, 9, 12, 16, 20,29, 39, 41,48, 49, 51 are amended. Claims 52-56 are newly added. Claims 1-9, 11-14, 16-27, 29-51 and newly added claims 52-56 are pending. Claims 3-8, 18-19, 23-27, 31-38, 40, 42-46 and 50 are withdrawn with traverse (the response filed 8/7/06) from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim.

3. Claims 1-2, 9, 11-14, 16-17, 20-22, 29-30, 39, 41, 47-49 and 51-56 are under examination with respect to prion, BSE, peroxynitrite and antibody in this office action.

4. Any objection or rejection of record, which is not expressly repeated in this office action, has been overcome by Applicant's response.

5. Applicant's arguments filed on 10/9/09 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections/Objections Withdrawn

6. The objection to claim 30 is withdrawn in response to Applicant's correction on the claim status.

The objection to claim 49 under 37 CFR 1.75 as being a substantial duplicate of claim 1 is withdrawn in response to Applicant's amendment to the claim and arguments on p. 21.

Claim Rejections/Objections Maintained

In view of the amendment filed on 10/9/09, the following rejections are maintained.

Claim Rejections/Objections

7. Claims 56 objected to because of the following informalities: An article "an" in line 5 before "accessible" in claim 1 is missing, an article "an" in line 7 before "accessible" in claim 39 is missing, an article "an" in line 5 before "accessible" in the claim 49 is missing and an article "an" in line 11 before "antibody" in the claim 56 is missing.. Appropriate correction is required.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 9, 11-14, 16-17, 20-22, 29-30, 39, 41, 47-49 and 51-56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for detecting more epitopes recognized by antibodies 6H4 and 3F4 in prion protein PrP or a mutant PrP^{Sc} in brain homogenate treated with acid and peroxynitrite in the presence of guanidine then mock treated brain homogenate by immunoprecipitation using antibodies 6H4 and 3F4, does not reasonably provide enablement for the claimed method of detecting whether a structurally and functionally undefined candidate polypeptide with a unknown target epitope is in a wild-type or aggregated or misfolded conformation by using an unknown chemical modifying agent to block a unknown accessible epitope in the polypeptide, disaggregating or denaturing the candidate protein, and determining whether the modified protein is in a wild-type or aggregated or misfolded conformation as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The rejection is maintained for the reasons made of record.

Claims 1-2, 9, 11-14, 16-17, 20-22, 29-30, 39, 41, 47-48 and 51-56 as amended are drawn to a method of detecting whether a candidate polypeptide including a target epitope is in a wild-type or aggregated or misfolded conformation by comprising contacting the polypeptide (including Prion polypeptide) with a chemical modifying agent (including peroxynitrite) to block an accessible epitope wherein in the wild type conformation, the target epitope is accessible and reacts with the blocking agent; and wherein in the aggregated or misfolded conformation, the target epitope is inaccesible

and the target epitope cannot react with the blocking agent, removing the unreacted chemical modifying agent, disaggregating or denaturing the candidate to convert any inaccessible target epitope to accessible target epitope and contacting the polypeptide with an aptamer or antibody to determine whether the polypeptide is in a wild type or in an aggregated or misfolded conformation. Claim 49 as amended is drawn to a similar method as set forth above except that wherein in the wild type conformation, the target epitope is inaccessible and cannot react with the blocking agent; and wherein in the aggregated or misfolded conformation, the target epitope is accessible and reacts with the blocking agent.

On p. 13-18 of the response, Applicant argues that it is not required to disclose all of the target epitopes, candidate polypeptides, blocking and detection agents in the claimed method in order to enable the claims. Applicant further cites Example C in the USPTO enablement training materials. Applicant argues that instant claims are enabled for the full scope of the claimed invention because the specification teaches several chemical modifying agents on p. 16 and working examples in figures 1-5. Applicant argues that specifications teaches a candidate polypeptide that comprises prion protein also teaches APP, SOD1, alpha-synuclein, islet amyloid polypeptide, resistin and p53 in figures 1-5 and prophetic example for Tau. Applicant argues that the specification provides several examples, defined epitopes, and different blocking agents. Applicant argues that the instant specification teaches a number of target epitopes on p. 38 and how to identify target epitopes on 34-35 and SOD1 target epitopes in Example 9, and

working examples also teach epitopes in PrP recognized by 3F4 and 6H4 antibody and epitopes in Abeta recognized by 6E10 and optimization parameters in Example 4. Applicant argues that the specification teaches the structural relationship between the Prion PrP and other polypeptides is conformation and the polypeptides are all related structurally in that they exist in a wild type folded conformation and also exist an aggregated or misfolded conformation. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, the instant specification fails to provide sufficient guidance as to enable a skilled artisan to practice the full scope of the claimed invention because the instant specification fails to teach how to make and use all of the structurally and functionally undefined targets epitopes, candidate polypeptides, blocking agents and detection agents in the claimed method. A skilled artisan cannot use several unknown or undefined agents to determine another unknown property or result. The skilled artisan cannot contemplate what targets epitopes, candidate polypeptides, blocking agents and detection agents are and whether they can be used to determine another unknown factor; i.e. whether the candidate polypeptides are in a wild type conformation or in an aggregated or misfolded.

Based on the specification and prior art, Applicant is enabled for a method of detecting prion protein PrP or PrP^{Sc} in brain homogenate using antibodies 3F4 and 6H4. In addition, Applicant is enabled for a method of detecting more epitopes recognized by antibodies 3F4 and 6H4 in acid and peroxynitrite treated brain homogenate in the presence of guanidine as compared to mock-treated brain homogenate. However, the

instant claims are not limited to the methods as set forth above. As previously made of record, independent claims 1, 39 and 49 encompass the detection of structurally and functionally undefined candidate polypeptides, structurally and functionally undefined target epitopes, inaccessible and accessible target epitopes, and also encompass the use of structurally and functionally undefined blocking agents and detection agents.

As previously made of record, independent claims fail to limit what the claimed candidate polypeptide is. Although the specification describes APP, SOD1, alpha-synuclein, islet amyloid polypeptide, resistin and p53 in figures 1-5 and prophetic example for Tau, the claims are not limited to the molecules as set forth above.

Although the specification is not required to disclose all of the claimed polypeptides and agents used in the claimed method, it is necessary to understand the functional and structural relationship between the known polypeptides and agents that can be used in the method and the unknown polypeptides and agents. However, the specification fails to teach the structural and functional relationship between the known candidate polypeptide (PrP) and other polypeptide and also fails to teach the relationship between acid/peroxynitrite/guanidine and other undefined agents. Thus it is unpredictable what other candidate polypeptide, epitopes, blocking agents and detection agents are and thus can be used in the claimed method.

The specification fails to teach the structurally and functionally relationship between the prion PrP and other unknown polypeptides. Although Applicant argues that structurally and functional relationship between the PrP and other unknown polypeptide is conformation, it is noted that if the candidate polypeptides are not structurally and

functionally defined, the conformation and target epitopes, accessible and inaccessible epitopes cannot be determined. Thus, it is unpredictable whether all of the structurally and functionally undefined candidate polypeptides, epitopes, blocking agents and detection agents can be used in the claimed method.

In addition, the claims fail to specify what the target epitopes, accessible and inaccessible epitopes are and what the blocking and detection agents are. Although the specification teaches prion PrP treated with acid and peroxynitrite in the presence of guanidine can be detected more epitopes recognized by antibodies 3F4 and 6H4, the claims fail to limit what target epitopes, accessible or inaccessible epitopes are and how they can be detected. The specification fails to teach what other detection agents or methods are except immunoprecitation of PrP with antibodies 3F4 and 6H4. The specification also fails to teach what other chemical modifying agent or blocking and detection agents are and thus can be use in the claimed method. The specification also fails to teach the structurally and functionally relationship between the epitopes recognized by antibodies 3F4 and 6H4 and other unknown epitopes, and nor does the relationship between 3F4/6H4 antibodies and other detection agents. Further, the specification also fails to teach the structurally and functionally relationship between peroxynitrite and other blocking agents or between acid or other modification method or agents. Thus, a skilled artisan cannot contemplate what polypeptides, epitopes, blocking agents, or detection agents are and whether they can be used in the claimed method and thus within the scope of the claims.

Note that the scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, it is unpredictable what changes can be made and still maintain activity; and thus the experimentation left to those skilled in the art is extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986). Thus, the skilled artisan cannot readily make and use the claimed invention as currently claimed without further undue experimentation. Note that

"The 'predictability or lack thereof' in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Accordingly, what is known in the art provides evidence as to the question of predictability. In particular, the court in In re Marzocchi, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971)" See MPEP § 2164.03.

Claim Rejections - 35 USC § 112

9. Claims 1-2, 9, 11-14, 16-17, 20-22, 29-30, 39, 41, 47-49 and 51-56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is maintained for the reasons made of record.

Claims 1-2, 9, 11-14, 16-17, 20-22, 29-30, 39, 41, 47-48 and 51-56 as amended are drawn to a method of detecting whether a candidate polypeptide including a target epitope is in a wild-type or aggregated or misfolded conformation by comprising

contacting the polypeptide (including Prion polypeptide) with a chemical modifying agent (including peroxynitrite) to block an accessible epitope wherein in the wild type conformation, the target epitope is accessible and reacts with the blocking agent; and wherein in the aggregated or misfolded conformation, the target epitope is inaccesible and the target epitope cannot react with the blocking agent, removing the unreacted chemical modifying agent, disaggregating or denaturing the candidate to convert any inaccessible target epitope to accessible target epitope and contacting the polypeptide with an aptmer or antibody to determine whether the polypeptide is in a wild type or in an aggregated or misfolded conformation. Claim 49 as amended is drawn to a similar method as set forth above except that wherein in the wild type conformation, the target epitope is inaccessible and cannot react with the blocking agent; and wherein in the aggregated or misfolded conformation, the target epitope is accesible and reacts with the blocking agent.

On p. 18-20 of the response, Applicant argues that instant claims meet the written description requirement because the specification provides numerous examples, working examples and a represent number of candidate polypeptides, blocking agents, modifying steps and detection agents for the claimed method. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, the specification only describes detecting more epitopes recognized by antibodies 3F4 and 6H4 in acid and peroxynitrite treated brain homogenate in the presence of guanidine as compared to mock-treated brain homogenate. The specification fails to teach what other defined polypeptides can be detected by the

claimed method in a specific manner; in particular, there is no specific structural and functional relationship between PrP and other proteins that can be detected by the claimed method. There is no information about what specific structure or amino acid sequences must be conserved for the claimed genus of structurally and functionally undefined candidate polypeptide, the genus of structurally and functionally undefined target epitope, accessible target epitope and inaccessible target epitope, the genus of blocking agent and the genus of detection agent. Since the functional and structural relationship between the claimed polypeptides and target epitopes with no defined structures and PrP is unknown, a skilled artisan cannot envision the functional correlations between the claimed genera and the claimed invention without specific information. Thus, the specification fails to reasonably demonstrate that Applicant is in possession of the claimed method to detect all of structurally and functionally undefined polypeptides or epitopes with undefined blocking agents.

Note that

A definition by function alone "does not suffice" to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." *Eli Lilly*, 119 F.3 at 1568, 43 USPQ2d at 1406. See also *Fiers*, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing *Amgen Inc. v.Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991)). An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., *Univ. of Rochester v. G.D. Searle &Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004).

In contrast, the specification provides an invitation for others to discover a representative number of species, or to discover what constitutes any particular portion of the structure that must be conserved, with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics. Thus,

Applicants were not in possession of the claimed method using structurally and functionally undefined candidate polypeptides, undefined target epitopes, accessible target epitopes and inaccessible target epitopes, undefined chemical modifying or blocking agents, and undefined detection agents or antibodies. Accordingly, the rejection is maintained.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-2, 9, 11-14, 16-17, 20-22, 29-30, 39, 41, 47-49 and 51-56 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 18-22 of U.S. Patent No. 7041807. The rejection is maintained for the reasons made of record, and as follows.

On p.21 of the response, Applicant argues that independent claims have been amended to recite "chemical modifying agent" that chemically reacts with selectively and blocks accessible target epitope and the claims of the '807 patent do not react a

chemical modifying agent with target epitope. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, the claims of the '807 patent are directed to a method for detecting PrP^{Sc} in a biological sample using an antibody that is able to recognize PrP^{Sc} wherein the antibody selectively binds to PrP^{Sc}. The '807 patent's method is a species that anticipates the generic claimed method because the claimed method is directed to a method of detecting all forms of polypeptides including PrP^{Sc} using all forms of detecting agents including antibodies against PrP^{Sc}. In addition, since the instant claims do not limit the chemical modifying agent, an agent that can change the biological property or denature the protein such as NP-40, Tween-20, proteinase K and SDS used in the method of the '807 patent in preparation of brain homogenates or PrP^{SC} protein for ELSAI or Western Blot meets the limitation of chemical modifying agent and thus anticipated the instant claims.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2, 9, 11-14, 16-17, 20-22, 29-30, 39, 41, 47-49 and 51-55 are rejected under 35 U.S.C. 102 (b) as being anticipated by US2002/0123072 (Prusiner et al. published Sep 5, 2002). Claims 1-2, 9-17, 20-22, 29-30, 39, 41, 47-49 and 51 stand rejected under 35 U.S.C. 102 (e) as being anticipated by US6677125 (Prusiner et al. issued Jan 13, 2004, priority Oct 9, 1998). These rejections are based on the subject mater that is enabled within the claims. The rejections are maintained for the reasons made of record.

Claims 1-2, 9, 11-14, 16-17, 20-22, 29-30, 39, 41, 47-48 and 51-55 as amended are drawn to a method of detecting whether a candidate polypeptide including a target epitope is in a wild-type or aggregated or misfolded conformation by comprising contacting the polypeptide (including Prion polypeptide) with a chemical modifying agent (including peroxynitrite) to block an accessible epitope wherein in the wild type conformation, the target epitope is accessible and reacts with the blocking agent; and wherein in the aggregated or misfolded conformation, the target epitope is inaccesible and the target epitope cannot react with the blocking agent, removing the unreacted chemical modifying agent, disaggregating or denaturing the candidate to convert any inaccessible target epitope to accessible target epitope and contacting the polypeptide with an aptamer or antibody to determine whether the polypeptide is in a wild type or in an aggregated or misfolded conformation. Claim 49 as amended is drawn to a similar method as set forth above except that wherein in the wild type conformation, the target epitope is inaccessible and cannot react with the blocking agent; and wherein in the

aggregated or misfolded conformation, the target epitope is accessible and reacts with the blocking agent.

On p. 21-22 of the response, Applicant argues that the claims have been amended to recite "chemical modifying agent that chemically reacts with target epitope" and Prusiner does not teach reacting a chemical modifying agent with target epitope. Applicant argues none of the various assays taught by Prusiner is embraced by the instant claims. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, the examiner asserts that Prusiner does teach the claimed method because Prusiner does teach "reacting a chemical modifying agent with a target epitope". In contrast to Applicant's arguments, Prusiner's assay does teach the step of contacting the polypeptide with a chemical modifying agent that reacts with and blocks an accessible target epitope as recited in instant claims 1, 39 and 49 because Prusiner teaches pretreatment of samples with antibodies binding to the non-disease conformation of the protein and remove the non-disease protein or pretreatment of samples with acids or alkaline or temperature or chemicals (i.e. chemical modifying agent that chemically reacts with the target epitope) to destroy proteins that are not related to the assayed proteins (see p. 7, [0099], in particular), which meets the limitation as recited in independent claims 1, 39 and 49 and dependent claims 9-14 (including non-elected species in claim 9).

Prusiner also teaches a method of detecting the presence of a disease related to conformation of a protein PrP^{Sc} (i.e. an aggregated or misfolded conformation) and a non-disease related conformation of the protein PrP^{C} (wild type conformation) in a sample using an antibody specific for PrP^{Sc} such as 3F4 or antibodies in WO97/10505 (see p. 4, [0042]-p. 5, [0049]; p.6, [0089]-p.7, [0097] ; p. 7, [0098]-p.8, [0103]; p. 11-14, examples 1-4; p.15, claims 1-27, in particular), which meets the limitations as recited in instant claims 1-2, 9, 11-14, 16-17, 20-22, 29-30, 39, 41, 47-48 and 51-55.

Prusiner teaches the detection of more PrP^{sc} in denature form of PrP (i.e. aggregated or misfolded conformation and then disaggregating or denaturing) than in native form with selected antibodies such as 3F4 (see p.9, [0110]-[[0116], in particular) and also teaches detection of aggregated or misfolded conformation of PrP as an indicator of prion disease as recited in instant claims 2, 20-22 (see p. 8, [0107]-p.9, [0109], in particular).

Prusiner also teaches that samples including brain or other biological samples are pre-treated and treated with acid, chemical or chaotropic salts, denaturing detergents, guanidine hydrochloride or proteinase to denature or unfold proteins as recited in instant claims 1-2, 9, 11-14, 16-17, 20-22, 29-30, 39, 41, 47-48 and 51-55 (see col.12-14, in particular). Thus, the teachings of Prusiner anticipate claims 1-2, 9, 11-14, 16-17, 20-22, 29-30, 39, 41, 47-48 and 51-55.

14. Claims 1-2, 9, 11-14, 16-17, 20-22, 29-30, 39, 41, 47-49 and 51-55 are rejected under 35 U.S.C. 102(e) as being anticipated by US7041807 (Cashman et al., issued May 9, 2006, priority Jun 23, 1999). The rejection is maintained for the reasons made of record.

On p. 23 of the response, Applicant argues that Cashman does not teach the claimed method because instant claims have been amended to recite "a chemical modifying agent that chemically reacts with a target epitope". Applicant's arguments have been fully considered but they are not persuasive.

In contrast, the claims of the '807 patent are directed to a method for detecting PrP^{Sc} in a biological sample using an antibody that is able to recognize PrP^{Sc} wherein the antibody selectively binds to PrPSc. The '807 patent's method is a species that anticipates the generic claimed method because the claimed method is directed to a method of detecting all forms of polypeptides including PrP^{Sc} using all forms of detecting agents including antibodies against PrP^{Sc}. In addition, since the instant claims do not limit the chemical modifying agent, an agent that can change the biological property or denature the protein such as NP-40, Tween-20, proteinase K and SDS used in the method of the '807 patent in preparation of brain homogenates or PrP^{SC} protein for ELSAI or Western Blot meets the limitation of chemical modifying agent and thus anticipated the instant claims (see col. 11-14; col. 18-19; col. 25-28, in particular). Thus the Cashman's method is a species that anticipates the generic claimed method as recited in instant claims because the claimed method is directed to a method of detecting all forms of polypeptides including PrP^{Sc} using all forms of detecting agents

including antibodies against PrP^{Sc} (see col. 11-14; col. 18-19; col. 25-28, in particular). Accordingly, the rejection of claims 1-2, 9, 11-14, 16-17, 20-22, 29-30, 39, 41, 47-49 and 51-55 under 35 U.S.C. 102(e) as being anticipated by US7041807 is maintained.

New Grounds of Rejection Necessitated by the Amendment

The following rejections are new grounds of rejections necessitated by the amendment filed on 10/9/09.

Claim Rejections - 35 USC § 112

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 9, 11-14, 16, 17, 20-22, 29-30, 41, 47-48, 51-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2, 9, 11-14, 16, 17, 20-22, 29-30, 41, 47-48, 51-55 are indefinite because claim 1 recites the limitation "the blocking agent" in lines 6-7 and line 9. There is insufficient antecedent basis for this limitation in the claim. The rest of the claims are indefinite as depending from an indefinite claim.

Conclusion

16. NO CLAIM IS ALLOWED.

17. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chang-Yu Wang, Ph.D.
December 2, 2009

/Chang-Yu Wang/
Examiner, Art Unit 1649